REMARKS:

This application is amended in manner that is believed to require further consideration and/or search. Accordingly, the amendment is being filed with a Request for Continued Examination.

The application is now believed to be in condition for allowance at the time of the next Official Action.

Status of the Claims

Claim 1 is amended to include the features of claim 3.

Claim 15 is amended to depend from claim 14.

Claims 7, 17 and 20 are amended as to form.

Claim 3 is cancelled.

1, 2 and 4-20 remain in this application.

Claim Rejections-35 USC §103

Claims 1, 4-9 and 18-20 stand rejected under 35 U.S.C. §103(a) as being unpatentable over WOHLSTADTER, et al. U.S. Patent No. 6,673,533 (WOHLSTADTER) in view of EL SHAMI et al. U.S. 4,778,751 (EL SHAMI) and NIWA et al. (NIWA).

Claims 2-3 and 11-17 were rejected under 35 U.S.C. §103(a) as being unpatentable over WOHLSTADTER in view of EL SHAMI and NIWA, further in view of PETTIT et al. U.S. 6,548,644 (PETTIT).

These rejections are together respectfully traversed for the reasons below.

With respect to independent claim 1, WOHLSTADTER fails to suggest at least of the four features of claim 1:

- **An interdigital electrode with a counter-electrode**.

The claimed biosensor includes a counter-electrode in combination with an interdigital electrode on the same substrate.

WOHLSTADTER, however, discloses an interdigital electrode that is identical to both the counter electrode and working electrode, for example as shown in Figure 19.

- **The spacing between the electrode pairs of the interdigital electrode**.

The claimed biosensor includes at least one interdigital electrode pair structure of electrodes arranged in pairs accommodated on the silicon substrate with a spacing between the electrode pairs of maximum 1.0 μm.

WOHLSTADTER is silent to this feature.

- **The first protein layer**.

The claimed biosensor includes a first layer made of protein at least covering over the interdigital electrode structure, and the capture antibodies are immobilized over the

interdigital electrode structure by the protein of the first layer (i.e., as previously recited in claim 3).

WOHLSTADTER, however, discloses, for example, streptavidin-coated silica particles which are located on a fibril mat electrode in the description of Figure 49 in column 8. Accordingly, the electrochemical and chemical behavior of this protein coat is completely different than the protein coat on the interdigital electrode structure, which may be made of gold as further recited in claim 7.

WOLSTADTER also disclose, e.g. in column 102, this protein coat may be as a flat layer on a gold electrode on glass slides. Again, the electrochemical behavior and preparation of such layers are different from the first protein layer on the claimed interdigital electrodes as claimed.

- **The second protein layer.**

The claimed invention includes a second protein layer applied over the first layer, which includes the capture antibody corresponding to the detecting antigen and which can couple to the antigen.

WOHLSTADTER, however, does not describe such a structure (e.g., in column 22). Instead, there are many binding reagents described without any preference, whereby antibodies are one possible reagent out of these many binding reagents. A protein layer with antibodies on top of a first protein layer is

not described. In column 35, for example, WOHLSTADTER discloses a redox active species immobilized on a fibril mat, and in column 1 WOHLSTADTER discloses an enzyme linked to immunoassay. However, there is no biosensor described where an antigen is coupled to the capture antibody and by means of an enzyme-marked detection anti-body also coupled to the antigen, redox-reactive molecules are enzymatically released on a sensor surface.

To remedy these shortcomings, SHAMI and NIWA were offered, and PETTIT was relied for teaching "the capture antibodies are immobilized over the interdigital electrode structure by the protein of the first layer", which was previously recited in claim 3.

EI SHAMI was offered for teaching "a method of detecting allergen-specific IgE by coupling a sample of human blood serum suspect of containing the allergen-specific IgE to an immobilized allergen on a solid support followed by coupling a labeled anti-IgE antibody to the allergen-specific IgE".

The position maintained was that it would have been obvious to include in the biosensor of WOHLSTADTER "with the antigen detection method of El Shami, *et al.* in order to detect antigens from various samples, including those derived from human blood."

However, there is no explanation of (1) how EL SHAMI is intended to modify the structure of WOHLSTADTER or (2) why one would have looked to EL SHAMI to modify WOHLSTADTER.

It is respectfully noted that "[R]ejections on obviousness cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness." KSR, 550 U.S. at ___, 82 USPQ2d at 1396 quoting In re Kahn, 441 F.3d 977, 988, 78 USPQ2d 1329, 1336 (Fed. Cir. 2006).

Indeed, these two documents are not related. The purpose of WOHLSTADTER is to provide a patterned multi-array, multi-specific surface (PMAMS) for electrochemiluminescence based tests. The objective is to provide a cost effective and disposable electrode for conducting such assays. See, e.g., the Introduction in column 1 and the Objects of the Invention in column 3.

However, EL SHAMI is concerned with the measurement of circulating antigens or antibodies in biological fluids, and EL SHAMI discloses that the teachings could be used to "prepare efficient solid phase matrices by attaching antigens or antibodies to a liquid matrix and labeling said matrix with a given liquid then pre-reacting said matrix with a solid phase support containing an anti-ligand".

EL SHAMI is interested in a different technique, and, thus, one of ordinary skill in the art would have had no reason to consider EL SHAMI to modify WOHLSTADTER.

NIWA was offered for disclosing an interdigitated array described usable for redox-cycling, which includes a gap size between the electrodes within the claimed range. The position was maintained was that it would have been obvious "to include in the biosensor of Wohlstadter, *et al.* with the IDA electrode geometric configuration of Niwa, *et al.* in order to increase collection efficiency as taught by Niwa, *et al.*"

However, there is no protein layer assembly or antigen/antibody detection described. With the exception of the interdigital electrodes on silicon, there are no features of the present claim 1 in NIWA. Thus, there would not have been an expectation of success of substituting the electrode of NIWA for electrode of WOHLSTADTER, as the over all structure is different.

PETTIT was offered, among other reasons, for teaching the proteins of the first protein layer, the binding partners of the first and second protein layers and the type of antigen.

PETTIT describes, at column 2, lines 26 to 33, a method to protect a protein with the help of ethylene glycol. This is done in a column as used, for example, in chromatography (column 6, lines 46 to 48). However, PETTIT fails to suggest use in an electrochemical sensor. For example, binding a molecule on plane such as an interdigital electrode is different than binding a molecule on a powder in a chemical column. As stated in PETTIT, column 6, lines 56 to 58, antibodies have a spatial orientation which provides for their maximal binding with the protein

selected for conjugation. The orientation, however, is not optimized for electrochemical detection reactions.

PETTIT teaches a solid support (powder in a column) with immobilized protein, for example protein A or G, and antibodies binding to the protein by the Fe domain to protect the protein (column 6, lines 46 to 58).

Amended claim 1 recites a silicon substrate with interdigital electrodes covered by a first protein, capture antibodies immobilized by the first protein layer and a selective second protein layer with a selected capture antibody corresponding to the detecting antigen.

Therefore the function and layer form of the protein/antibody in claim 1 is totally different to that of PETTIT. One person skilled in the art would not use the system in PETTIT, where an antibody is protecting a protein, to form a sensor in which an antibody applied to one first protein layer is increasing selectivity of a second protein layer. Also a flat electrode surface is different to a powder in a column. A column is also different in function, construction and reaction mechanism compared with an electrochemical sensor.

In view of the above remarks SHAMI, NIWA and/or PETTIT do not prompt one to modify WOHLSTADTER so as to even approach the claimed structure. Indeed, even if one were to combine these documents, there is no description of an electrochemical

detection or electrodes, protein layers systems, redox reactive molecules as described by the claimed invention, e.g., claim 1.

Therefore, the proposed combination fails to render obvious independent claim 1 and dependent claims 2 and 4-13 and 16-20, and withdrawal of the rejection is respectfully requested.

As to method claims 14 and 15, the combination of WOHLSTADTER, EL SHAMI and NIWA fail to teach or suggest a method as claimed for the reasons discussed above, as the method includes the biosensor structural features as described in claim 1.

Therefore, the combination of WOHLSTADTER, EL SHAMI and NIWA with PETTIT fails to render obvious claims 14 and 15, and withdrawal of the rejection is respectfully requested.

Conclusion

In view of the amendment to the claims and the foregoing remarks, this application is in condition for allowance at the time of the next Official Action. Allowance and passage to issue on that basis is respectfully requested.

Should there be any matters that need to be resolved in the present application, the Examiner is respectfully requested to contact the undersigned at the telephone number listed below.

The Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to our credit card which is being paid online simultaneously herewith for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17.

Respectfully submitted,

YOUNG & THOMPSON

/Robert A. Madsen/
Robert A. Madsen, Reg. No. 58,543
209 Madison Street, Suite 500
Alexandria, VA 22314
Telephone (703) 521-2297
Telefax (703) 685-0573
(703) 979-4709

RAM/fb